CLAIMS

1. A method of imaging hypoplastic, anatomically displaced or ectopic cells or tissues in a mammalian subject by scintigraphic or magnetic resonance imaging, comprising the steps of: (a) parenterally injecting a mammalian subject, at a locus and by a route providing access to an organ of interest, with an antibody or antibody fragment which specifically binds a marker produced by or associated with said cell or tissue, said antibody or antibody fragment being labeled with a radioisotope or with a magnetic resonance image enhancing agent capable of external detection, the amount of the labeled antibody or antibody fragment being sufficient to permit a scintigraphic image or an enhanced magnetic resonance image of said organ to be obtained; and (b) obtaining a positive scintigraphic image or positive enhanced magnetic resonance image of said organ, at a time after injection of said agent sufficient for said agent to diffusely accrete in said organ and specifically bind to said marker.

2. The method of claim 1 wherein the cell or tissue is pretargeted with a first composition comprising a streptavidin-conjugated antibody, biotinylated antibody to be used in conjunction with avidin and biotin, bifunctional antibody, antibody-hapten complexes, or enzyme-conjugated antibody, wherein the antibody is an antibody or antibody fragment which specifically binds a marker produced by or associated with said cell or tissue, and after the first composition accretes at the targeted tissue or cell, a second composition, which bears the imaging principle, is administered which activates the first composition or couples with the first composition to produce a desired effect.

3. The method of claim 1 wherein the isotope emits at 50-1,500 kev energy.

4. The method of claim 1 wherein the mri enhancing agent is a species of Gadolinium, Iron, Manganese, Rhenium, Europium, Lanthanium, Holmium, or Ferbium.

5. The method of claim 2, wherein the cell or tissue is pretargeted by injecting the subject with the first composition which comprises biotinylated antibody or fragment, optionally injecting the patient with a clearing composition comprising an agent to clear circulating biotinylated antibody or fragment, and then injecting the second composition which comprises biotin conjugated with isotope or mri enhancing agent.

6. The method of claim 1 wherein the antibody is a Fv, single chain antibody, Fab, Fab', or $F(ab')_2$ fragment or intact antibody.

7. The method of claim 1 wherein the antibody or fragment has a specific immunoreactivity to targeted cells or tissues of at least 60% and a cross-reactivity to other antigens of less than 35%.

8. A method for detecting organ tissue retained after surgical removal of a portion of the organ, wherein the organ tissue produces or is associated with a marker substance, the method comprises injecting a human subject parenterally with an antibody specific to the marker substance and radiolabeled with a pharmacologically inert radioisotope or magnetic resonance imaging agent capable of detection using a photoscanning or magnetic resonance imaging device.

9. The method of claim 8 wherein the cell or tissue is pretargeted with a first composition comprising a streptavidin-conjugated antibody, biotinylated antibody used in conjunction with avidin and biotin, bifunctional antibody, antibody-hapten complexes, or enzyme-conjugated antibody,

wherein the antibody is an antibody or antibody fragment which specifically binds a marker produced by or associated with said cell or tissue, and after the first composition accretes at the targeted tissue or cell, a second composition, which has the imaging agent, is administered which activates the first composition or couples with the first composition to produce a desired effect.

10. The method of claim 8 wherein the isotope emits at 50-1,500 kev energy.

11. The method of claim 8 wherein the mri enhancing agent is a species of Gadolinium, Iron, Manganese, Rhenium, Europium, Lanthanium, Holmium, or Ferbium.

12. The method of claim 9, wherein the cell or tissue is pretargeted by injecting the subject with the first composition which comprises biotinylated antibody or fragment, optionally injecting the patient with a clearing composition comprising an agent to clear circulating biotinylated antibody or fragment, and then injecting a second composition which comprises biotin conjugated with isotope or mri enhancing agent.

13. The method of claim 8 wherein the antibody is a Fv, single chain antibody, Fab, Fab', or $F(ab')_2$ fragment or intact antibody.

14. The method of claim 8 wherein the antibody or fragment has a specific immunoreactivity to targeted cells or tissues of at least 60% and a cross-reactivity to other antigens of less than 35%.

15. A method for determining in a mammal, a first organ's condition, the first organ producing or being associated with a marker substance and being adjacent to a second organ which

has been surgically removed from the mammal; the method comprising injecting the mammal parenterally with an antibody specific to the marker substance and radiolabeled with a pharmacologically inert radioisotope or magnetic resonance imaging agent capable of detection using a photoscanning or magnetic resonance imaging agent device, wherein the condition of the first organ is determined.

16. The method of claim 15 wherein the organ is pretargeted with a first composition comprising a streptavidin-conjugated antibody, biotinylated antibody used in conjunction with avidin and biotin, bifunctional antibody, antibody-hapten complexes, or enzyme-conjugated antibody, wherein the antibody is an antibody or antibody fragment which specifically binds a marker produced by or associated with said organ, and after the first composition accretes at the targeted tissue or cell, a second composition, which bears the imaging agent, is administered which activates the first composition or couples with the first composition to produce a desired effect.

17. The method of claim 15 wherein the isotope emits at 50-1,500 kev energy.

18. The method of claim 15 wherein the mri enhancing agent is a species of Gadolinium, Iron, Manganese, Rhenium, Europium, Lanthanium, Holmium, or Ferbium.

19. The method of claim 16, wherein the organ is pretargeted by injecting the subject with the first composition which comprises biotinylated antibody or fragment, optionally injecting the patient with a clearing composition comprising an agent to clear circulating biotinylated antibody or fragment, and then injecting the second composition which comprises biotin conjugated with isotope or mri enhancing agent.

20. The method of claim 15 wherein the antibody is a Fv, single chain antibody, Fab, Fab', or $F(ab')_2$ fragment or intact antibody.

21. The method of claim 15 wherein the antibody or fragment has a specific immunoreactivity to targeted cells or tissues of at least 60% and a cross-reactivity to other antigens of less than 35%.

22. A method for treating hypoplastic or ectopic tissue which produces or is associated with a marker substance, which comprises injecting a human subject parenterally with an antibody specific to the marker substance and conjugated with a cytotoxic agent.

23. The method of claim 22 wherein the cell or tissue is pretargeted with a first composition comprising a streptavidin-conjugated antibody, biotinylated antibody used in conjunction with avidin and biotin, bifunctional antibody, antibody-hapten complexes, or enzyme-conjugated antibody, wherein the antibody is an antibody or antibody fragment which specifically binds a marker produced by or associated with said cell or tissue, and after the first composition accretes at the targeted tissue or cell, a second composition is administered which activates a therapeutic agent on the first composition or couples a therapeutic agent to the first composition to produce a therapeutic effect.

24. The method of claim 22 wherein the therapeutic agent is an isotope, drug, toxin, fluorescent dye activated by nonionizing radiation, hormone, autocrine or cytokine.

25. The method of claim 22 wherein the isotope emits at 50-1,500 kev energy.

26. The method of claim 23, wherein the cell or tissue is

pretargeted by injecting the subject with the first composition which comprises biotinylated antibody or fragment, optionally injecting the patient with a clearing composition comprising an agent to clear circulating biotinylated antibody or fragment, and then injecting the second composition which comprises biotin conjugated with isotope.

27. The method of claim 22 wherein the antibody is a Fv, single chain antibody, Fab, Fab', or $F(ab')_2$ fragment or intact antibody.

28. The method of claim 22 wherein the antibody or fragment has a specific immunoreactivity to targeted cells or tissues of at least 60% and a cross-reactivity to other antigens of less than 35%.

29. The method of claim 22 wherein the antibody is a Fv, single chain antibody, Fab, Fab', or $F(ab')_2$ fragment or intact antibody.

30. The method of claim 22 wherein the tissue is ectopic.

31. The method of claim 30 wherein the ectopic tissue is endometrium.

32. Method for ablating non-malignant cells or tissues in a patient, the method comprising treating the patient with an antibody or antibody fragment specific to a marker associated with or produced by the cell to be ablated and which is conjugated to a cytotoxic agent.

33. The method of claim 32 wherein the therapeutic agent is an isotope, drug, toxin, fluorescent dye activated by nonionizing radiation, hormone, autocrine or cytokines.

34. The method of claim 32 wherein the antibody is a Fv,

single chain antibody, Fab, Fab', or $F(ab')_2$ fragment or intact antibody.

35. The method of claim 32 wherein the antibody or fragment has a specific immunoreactivity to targeted cells or tissues of at least 60% and a cross-reactivity to other antigens of less than 35%.

36. The method of claim 33 wherein the isotope is Iodine-125, Iodine-131, Rhenium-186, Rhenium-188, Silver-111, Platinum-197, Palladium-109, Copper-67, Phosphorus-32, Phosphorus-33, Yttrium-90, Scandium-47, Samarium-153, Lutetium-177, Rhodium-105, Praseodymium-142, Praseodymium-143, Terbium-161, Holmium-166, or Gold-199.

37. The method of claim 33 wherein the cytotoxic agent is taxol, mechlorethamine, cyclophosphamide, melphalan, uracil mustard, chlorambucil, thiotepa, busulfan, carmustine, lomustine, semustine, streptozocin, dacarbazine, methotrexate, fluorouracil, cytarabine, azaribine, mercaptopurine, thioguanine, vinblastine, vincristine, dactinomycin, daunorubicin, doxorubicin, bleomycin, mithramycin, mitomycin, L-asparaginase, cisplatin, hydroxyurea, procarbazine, mitotane, prednisone, hydroxyprogesterone caproate, medroprogesterone acetate, diethylstilbestrol, ethinyl estradiol, tamoxifen, and testosterone propionate or fluoxymesterone.

38. The method of claim 32 wherein the cell or tissue is pretargeted with a first composition comprising a streptavidin-conjugated antibody, biotinylated antibody used in conjunction with avidin and biotin, bifunctional antibody, antibody-hapten complexes, or enzyme-conjugated antibody, wherein the antibody is an antibody or antibody fragment which specifically binds a marker produced by or associated with said cell or tissue, and after the first composition accretes

at the targeted tissue or cell, a second composition is administered which activates a therapeutic agent on the first composition or couples a therapeutic agent to the first composition to produce a therapeutic effect.

39. The method of claim 33, wherein the cell or tissue is pretargeted by injecting the subject with the first composition which comprises biotinylated antibody or fragment, optionally injecting the subject with a clearing composition comprising an agent to clear circulating biotinylated antibody or fragment, and then injecting the second composition which comprises biotin conjugated with isotope.

40. Method for destroying bone-marrow cells in a patient prior to regrafting with normal bone marrow cells, the method comprising treating the patient with an antibody or antibody fragment specific to a marker associated with or produced by bone marrow cells and which is conjugated to a cytotoxic agent.

41. The method of claim 40 wherein the therapeutic agent is an isotope, drug, toxin, fluorescent dye activated by nonionizing radiation, hormone, autocrine or cytokine.

42. The method of claim 40 wherein the antibody is a Fv, single chain antibody, Fab, Fab', or $F(ab')_2$ fragment or intact antibody.

43. The method of claim 40 wherein the antibody or fragment has a specific immunoreactivity to targeted cells or tissues of at least 60% and a cross-reactivity to other antigens of less than 35%.

44. The method of claim 40 wherein the isotope is Iodine-125, Iodine-131, Rhenium-186, Rhenium-188, Silver-111, Platinum-197, Palladium-109, Copper-67, Phosphorus-32,

Phosphorus-33, Yttrium-90, Scandium-47, Samarium-153, Lutetium-177, Rhodium-105, Praseodymium-142, Praseodymium-143, Terbium-161, Holmium-166, or Gold-199.

45. The method of claim 40 wherein the cytotoxic agent is taxol, mechlorethamine, cyclophosphamide, melphalan, uracil mustard, chlorambucil, thiotepa, busulfan, carmustine, lomustine, semustine, streptozocin, dacarbazine, methotrexate, fluorouracil, cytarabine, azaribine, mercaptopurine, thioguanine, vinblastine, vincristine, dactinomycin, daunorubicin, doxorubicin, bleomycin, mithramycin, mitomycin, L-asparaginase, cisplatin, hydroxyurea, procarbazine, mitotane, prednisone, hydroxyprogesterone caproate, medroprogesterone acetate, diethylstilbestrol, ethinyl estradiol, tamoxifen, and testosterone propionate or fluoxymesterone.

46. A sterile injectable composition for human use comprising an antibody or antibody fragment specific to an antigen associated with or produced by non-malignant cells, conjugated with a cytotoxic agent in a pharmaceutically acceptable sterile injection vehicle.

47. A sterile injectable composition for human use comprising an antibody or antibody fragment specific to an antigen associated with or produced by bone marrow cells, conjugated with a cytotoxic agent in a pharmaceutically acceptable sterile injection vehicle.

48. An antibody or antibody fragment specific to an antigen associated with or produced by normal organs and tissues, which is conjugated to an agent which is protective to the actions of the radiation and cytotoxic drugs to the organ and tissue.

49. The antibody or fragment of claim 48 wherein the antibody

is a Fv, single chain antibody, Fab, Fab', or $F(ab')_2$ fragment or intact antibody.

50. The antibody or antibody fragment of claim 48 wherein the cytoprotective agent is WR-2721 or WR-1065.

51. An improved method of therapy of cancer, wherein a human patient suffering from a cancer susceptible to treatment with radiation or a cytotoxic agent is treated with a therapeutic amount of radiation or a cytoxic agent,

the improvement comprising administering to said patient a cytotoxic-protective agent conjugated to an antibody or antibody fragment which specifically binds to an antigen which is produced by or associated with a normal cell which is to be protected from the cytotoxicity of the cancer therapy.

52. The method of claim 51 wherein the cytotoxic-protective agent is WR-2721 or WR-1065.

53. The method of claim 51 wherein the cell or tissue is pretargeted with a first composition comprising a streptavidin-conjugated antibody, biotinylated antibody used in conjunction with avidin and biotin, bifunctional antibody, antibody-hapten complexes, or enzyme-conjugated antibody, wherein the antibody is an antibody or antibody fragment which specifically binds a marker produced by or associated with said cell or tissue, and after the first composition accretes at the targeted tissue or cell, a second composition is administered which couples a cytoprotective agent to the first composition to produce a cytoprotective effect.

54. The method of claim 53, wherein the cell or tissue is pretargeted by injecting the subject with the first composition which comprises biotinylated antibody or fragment, optionally injecting the patient with a clearing composition comprising an agent to clear circulating biotinylated antibody

or fragment, and then injecting the second composition which comprises biotin conjugated with cytoprotective agent.

55. A sterile injectable composition for human use comprising an antibody or antibody fragment specific to an antigen associated with or produced by normal organs and tissues conjugated with a cytoprotective agent in a pharmaceutically acceptable sterile injection vehicle.

56. The composition of claim 55 wherein the cytoprotective agent is WR-2721 or WR-1065.

57. A kit comprising, in a suitable container, (A) an antibody or antibody fragment conjugated with a cytoprotective agent, and (B) a sterile, pharmaceutically acceptable injectable vehicle for injection of (A).

58. The kit of claim 57 wherin the cytoprotective agent is WR-2721 or WR-1065.

59. A kit comprising, in a suitable container, (A) an antibody/ toxin or therapeutic agent conjugate, and (B) a sterile, pharmaceutically acceptable injectable vehicle for injection of (A).

60. A method of cancer therapy with a first antibody or fragment specific to an antigen produced by or associated with a cancer cell, the first antibody or fragment being labeled or conjugated to a radioisotope, drug or toxin, given in combination with a second antibody or antibody fragment specific to an antigen associated with or produced by normal cells and tissues, the second antibody or fragment being conjugated with a cytoprotective agent to protect the normal cells from the cytotoxicity of the cancer therapy.

61. The method of claim 60 wherein the cytoprotective agent

is WR-2721 or WR-1065.

62. A method of affecting a function of a non-malignant cell in a mammalian subject, the method comprising administering to the subject a composition comprising an antibody specific to a growth factor receptor or hormone receptor on the targeted cell, wherein the antibody affects the function and proliferation of the cell.

63. A method of treating a condition affecting non-malignant calls in a mammalian subject, the method comprising administering to a subject requiring such treatment, a composition comprising an antibody or fragment specific to a hormone receptor or growth factor on a targeted cell, wherein the antibody or fragment is conjugated to a therapeutic agent.

64. A therapeutic conjugate comprising an antibody or fragment specific to a growth factor receptor or hormone receptor and a therapeutic agent.

65. The therapeutic conjugate of claim 64 wherein the therapeutic agent is an isotope, drug, toxin, hormone antagonist, cytokine, autocrine, or fluorescent dye activated by nonionizing radiation.

66. An immunological method of affecting a hormonal function of a cell in a mammalian subject, the method comprising administering to the subject a composition comprising an antibody or fragment specific to a hormone receptor on a targeted cell, wherein the antibody or fragment affects the hormonal function of the targeted cell.

67. The method of claim 66 wherein the antibody or fragment is conjugated to a therapeutic agent.

68. The method of claim 66 wherein the hormonal cell is of

the ovary, breast, or testis.

69. The method of claim 68 wherein the receptor is an FSH receptor or an LH receptor.

70. The method of claim 69 wherein the affected hormonal function produces amenorrhea or sterility.

71. The method of claim 66 wherein the receptor is an FSH or estrogen receptor.

72. The method of claim 71 wherein the affect is to treat fibrocystic breast disease.

73. The method of claim 66 wherein the hormone-dependent cell is of the prostate.

74. The method of claim 73 wherein the receptor is an androgen receptor.

75. An immunological method of ablating a cell in a mammalian subject, the method comprising administering to the subject requiring ablation of a cell, a composition comprising an antibody or fragment specific to a hormone receptor or growth factor receptor on a cell targeted for ablation, wherein the antibody or fragment is conjugated to a chemical or radiation ablation agent.

76. The method of claim 75 wherein the antibody to ovarian cell or receptor thereof is used to ablate or reduce the ovaries or its function.

77. The method of claim 75 wherein the antibody to prostate cells or receptor thereof is used to ablate or reduce the prostate or its functions.